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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,869	09/23/2003	Cyrus Rustam Kumana	UHK 00091	5138

23579 7590 03/20/2008

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EXAMINER	
CHOI, FRANK I	
ART UNIT	**PAPER NUMBER**
1616	

MAIL DATE	DELIVERY MODE
03/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,869	KUMANA ET AL.	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9,28-34 and 38-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,9,28-34 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20071102*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

As a preliminary matter, the Examiner had indicated in prior interview (9/6/2007), interview summary mailed on 9/21/2007, that an amendment to the method claims indicating that the side effect at issue was cardiac arrhythmia. However, as indicated below, the Applicant has not sufficiently shown that there is sufficient written description support for the claim amendment for the following reasons: (1) the citation to example 2 is insufficient to provide support as the Applicant fails to specifically indicate what disclosure in example 2 supports the amendment; (2) paragraph 0107 of the published application does not support the amendment because the same indicates that orally administered arsenic trioxide was comparable to intravenously administered arsenic trioxide in terms of cardiac arrythmias; (3) the evidence submitted by the Applicant, i.e the declaration (8/1/2007) and Kumana et al. (2002), are not the Specification and, in any case, do not show that at the time the Application was filed that the inventors contemplated the claim invention as amended; and (5) the Siu et al. (2006) which is a publication of the data set forth in the declaration (8/1/2007) appears to provide evidence that the inventors did not contemplate the claimed invention as amended until after the filing date the application.

Double Patenting

Applicant is advised that should claim 6 be found allowable, claim 44 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). There does not appear to be any difference in scope between claim 6 in which the dosage formulation of claim 1 further

comprises at least one additional pharmacological agent which is a chemotherapeutic and claim 44 in which the dosage formulation of claim 1 is combined with one or more additional chemotherapeutic agents.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 9, 28-34, 38-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With respect to claims 28-34, 38-45, the Applicant claims that oral administration of an arsenic trioxide composition produces a lower peak plasma concentration with less cardiotoxicity in the form of cardiac arrhythmias than the same amount of arsenic trioxide administered intravenously. The Applicant cites to Example 2 as support for said limitation. However, the inventors in paragraph 107 of the published application (US 2004/0126434) states as follows:

> Cardiac arrhythmias were not found, which was similar to a previous study of intravenous-As_2O_3 in Chinese patients, where arrhythmia was seen in only 1/58 patients (Niu C. et al., supra.).

Furthermore, in the paragraphs immediately following the above paragraph, the inventors disclose that the safety profile of oral arsenic trioxide is comparable to intravenous arsenic trioxide.

> [0108] It is important to note that only four patients received oral-As_2O_3 as a single agent for CR induction, with the rest having received ATRA or idarubicin before CR was reached. With this limitation, our results showed that oral-As_2O_3 had a short-term efficacy and safety profile similar to intravenous-As_2O_3. A recent study also showed that oral tetra-arsenic tetra-sulphide was highly efficacious in APL (Lu D. P. et al. Tetra-arsenic tetra-sulfide for the treatment of acute promyelocytic leukemia: a pilot report. Blood 2002;99:3136-43). However, the long-term efficacy and safety of oral-As_2O_3 as compared with intravenous-As_2O_3 will require longer follow-up.
>
> [0109] Finally, although oral- or intravenous-As_2O_3 and hematopoietic stem cell transplantation are effective treatment modalities for patients with relapsed APL, their relative merits are undefined, and further randomized trials will be needed to address this issue.

The Applicant cannot rely on the declaration (8/1/2007) or Kumana et al. (2002) because the rejection herein is based on lack of written description not enablement. The issue of written description is different from the issue of enablement. *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n- propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir.

2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion"). In this case, the disclosure above does not disclose that oral arsenic trioxide compositions have less cardiotoxicity in the form of cardiac arrythmias than the same amount of arsenic trioxide administered intravenously. The disclosure clearly indicates that oral arsenic trioxide and intravenous arsenic trioxide have comparable safety profiles.

With respect to the lower peak plasma concentration, the Applicant does not cite to any specific disclosure in Example 2 which supports the limitation that oral administration produces a lower peak plasma concentration. Example 2 appears to only discuss the AUC not peak plasma concentration. Furthermore, the declaration (8/1/2007) only tests oral administration, as such, there does not appear to be any comparison of peak plasma concentration between orally administered and intravenously administered arsenic trioxide.

Finally, it appears that the inventors did not contemplate that less cardiotoxicity in terms of cardiac arrhythmia was a function of lower peak concentration until after the present Application was filed. See Siu et al. (2006) (indicating that lower peak plasma arsenic reached during oral As2O3 may explain relative cardiac safety of oral As2O3). The Examiner notes that even if the result of administering oral arsenic trioxide to a human having acute myeloid leukemia, i.e relative lower peak plasma levels with less cardiotoxicity than the same amount of arsenic trioxide administered intravenously, was an inherent result of said administration, the same would not provide written description support as there is no explicit description in the

Specification at the time the application was filed that shows that the inventors contemplated the invention in terms of said result. See *Purdue Pharma L.P. v. Faulding Inc.*, cited above.

Additionally, with respect to claim 2, 3, claims 2 and 3 as originally filed were process limitations in which an arsenic trioxide solution was prepared by dissolving arsenic trioxide powder in solution. There does not appear to be any disclosure in the Specification, as originally filed, which discloses the subject matter of claims 2 and 3 separate from the arsenic trioxide solution. With respect to claim 9, claim 9 as originally filed was directed to a solution having an arsenic trioxide concentration of 1 mg/ml. Other than with respect to solutions and suspensions (Paragraphs 0032 and 0052 of the published application), the Specification does not appear to disclose the subject matter of claim 9, i.e. the subject matter constitutes new matter with respect to tablets, capsules and dispersions (but only to the extent that dispersions encompass formulations that are not solutions or suspensions). With respect to claims 28-30, to the extent that claims 29-30 include within its scope that the arsenic trioxide composition can be administered in the form of a powder, the same constitutes new matter. Claim 28 as originally filed was directed to a method of treating hematological malignancies with an arsenic trioxide composition that was prepared as a solution, with claims 29 and 30, as originally filed, indicating that said solution was prepared by dissolving arsenic trioxide powder in a solution. There does not appear to be any disclosure in the Specification, as originally filed, which indicates that the arsenic trioxide composition is administered as a powder per se (See paragraphs 0023, 0031,0032, 0049-0053 of the published application).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3,9 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 2 and 3, which are dependent on claim 1, if arsenic trioxide powder is the final form, it is unclear how arsenic trioxide can be a powder if arsenic trioxide is in the form of a tablet, capsule, dispersion or suspension as required by claim 1. The Applicant should clarify that arsenic trioxide powder is used in the preparation of the tablet, capsule, dispersion or suspension. In claim 9, it is unclear how a tablet and a capsule, which the specification does not appear to disclose any other contents than a powder composition, i.e. solid dosage forms, can have an arsenic trioxide concentration of 1 mg/ml (which are disclosed by the specification relative to solutions and suspensions). The Applicant should clarify that it is the dispersion or suspension that has an arsenic trioxide concentration of 1 mg/ml.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

> such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

With respect to the discussion of "dispersions" below, "dispersions" are not defined by the Applicant, and, as such, encompass a broad range of mixtures, including solutions, suspensions and even solids in solids. See Remington's (17th Ed. 1985), pp. 207, 301.

Claims 1-3, 9, 28-34, 38-42, 45 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Kumana et al. (published online October 11, 2002, received May 13, 2002, accepted August 22, 2002) expressly disclose a method of treating acute myeloid leukemia with a 10 mg dose of arsenic trioxide by administering an oral solution of arsenic trioxide having a concentration of 1 mg/ml which was prepared by mixing arsenic trioxide powder having a minimum purity of 99% in water and adjusting to a pH of 8 and subsequently making a final volume of 500 ml by adding dilute HCl and water to arrive at a pH of 7.2 (See entire document). A solution is not excluded by the limitation "dispersion" since a solution constitutes a dispersion at a molecular level. With respect to claim 31 is not clear that the limitation "incompletely" modifies both "dissolved" and "dispersed in solution", as such, the Examiner interprets claim 31 to include arsenic trioxide which is "dispersed in a solution". The rejection of claims 28-34, 38-42, 45 assumes that the observations and conclusions in Siu et al. (Blood, 1st ed. paper, 2006) are valid (See Siu et al., page 11 (limitations of the study)) such that the relative lower peak plasma concentration with less cardiotoxicity in the form of cardiac arrythmias than the same amount of arsenic trioxide administered intravenously is an inherent result of administering 10 mg dose of the arsenic trioxide solution above to a human. See Siu et al. (2006), page 105, page 106, note 11. The listed inventors of the present application, Kumana and Kwong, are only two of the

seven authors listed for Kumana et al. (2002), as such, the inventive entity of the present application and the reference are not the same. As such, the claimed invention appears to have been invented by other than the applicant.

Claims 28, 32, 38-42 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Siu et al. (Blood, 1st ed. paper, 2006) expressly discloses that oral As2O3 has lower peak plasma arsenic concentrations compared with intravenous As2O3 and a method of treating acute promyelocytic leukemia with 10 mg/d of oral arsenic trioxide (As2O3) in which ventricular proarryhthmia in all patients in the study test group was absent compared to the historical rate of torsades de pointes of 1% in patients receiving intravenous arsenic trioxide (Pages 1, 3, 10). The rejection of the claims assumes that the results and observations of Sui et al. are valid considering the limitations of the study, i.e., absence of a intravenous arsenic trioxide control group, previous reports of intravenous As2O3 have not measured QT dispersion, HRV, and circadian QT and HR variations (so how they relate to arrhythmias during intravenous As2O3 is difficult to judge) and a 1% frequency of torsades de pointes in intravenous As2O3 might not have been detected in the study size (Page 11). The listed inventors of the present application, Kumana and Kwong, are only two of the seven authors listed for Siu et al., as such, the inventive entity of the present application and the reference are not the same. As such, the claimed invention appears to have been invented by other than the applicant.

The Examiner withdraws the rejection of claims 1-3 over WO 99/24029 under 35 U.S.C. 102(b) or CN1370540 under 35 U.S.C. 102(a) for the sole reason that they are duplicative prior art.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamauchi et al.

Yamauchi et al. (1985) expressly disclose an oral dose of 4.5 mg/kg body weight (hamsters weighing 80 ± 7 g) of arsenic trioxide (Merck German; 99.96%) which had first been dissolved in a solution of NaOH and diluted with distilled water (Page 114).

Claims 2, 3 indicate that the arsenic trioxide is a powder, however, claim 1 requires that the dosage form be other than a powder, i.e. a tablet, capsules, dispersion or suspension. Further, claims 2 and 3 as originally filed in the context of claim 1 as originally filed were directed to product-by-process limitations and as, indicated above, the use of arsenic trioxide powder in the Specification is limited to preparation of solutions, suspensions and filling of capsules. As such, the Examiner reads claims 2 and 3 as being a process limitation in which the arsenic trioxide is provided as a powder during the preparation of the dosage formulation but the final formulation is a tablet, capsule, dispersion or suspension. As such, the prior art pill or tablet reads on claim 2. Additionally Claim 3 requires an arseniic trioxide purity of at least 90%, 95%, 96%, 97%, 98% or 99%, however, as indicated above, the purity limitation was in the originally filed claim was a product-by process limitation and the Specification only disclosed the same relative to the preparation of the aqueous arsenic trioxide solution (See Paragraphs 0023, 0030-0032 of the published application). In the final form, the arsenic trioxide will no longer be pure as it will be admixed with other ingredients to make the final form of a tablet, capsule, dispersion or suspension. As such, the Examiner reads claim 3 as being a process limitation in which the arsenic trioxide is provided having said purity in the preparation of the dosage formulation but the final formulation the arsenic trioxide no longer has said purity as it is admixed with other ingredients.

Claims 1-3,9 are rejected under 35 U.S.C. 102(e) as being anticipated by Ellison et al. (US Pat. 6,875,451).

Ellison et al. expressly disclose oral administration and administration as a pill or tablet of arsenic trioxide (Claims 6, 10, 11). An embodiment is expressly disclosed in which arsenic trioxide is dissolved in an aqueous solution of sodium hydroxide, with the pH adjusted to about 6-8 (Column 9, lines 33-36). A product of arsenic trioxide manufactured by Taylor Pharmaceuticals, Decatur, Ill. having a concentration of 1 mg/ml is expressly disclosed (Column 16, lines 15-17).

The discussion following the description of the relevant disclosure of Yamauchi et al. is incorporated herein to avoid repetition. Further, it is inherent that the arsenic trioxide solution from Taylor pharmaceuticals would have been prepared from dissolving arsenic trioxide powder and that said powder would be of sufficient purity to fall within the scope of the purity claimed in claim 3.

Claims 1-3, 28-32, 38, 40, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwong et al. (1997).

Kwong et al. expressly disclose a method of treating chronic myeloid leukemia with a Fowler's solution 5 minims/3 times a day (1 minim = 0.06 ml, equivalent to 0.6 mg As2O3) for 2 weeks (Page 3488, figure 1).

The discussion following the description of the relevant disclosure of Yamauchi et al. is incorporated herein to avoid repetition. Further, Claims 29 and 30 are interpreted similarly to claims 2 and 3. Claim 31 does not clearly indicate that "incompletely" modifies "dispersed in a solution", as such, the prior art solution reads on the claimed invention. As indicated above, assuming that Sui et al. is valid, the rejection of claims 28-32, 38, 40, 45 are based on the inherent result, i.e. that the orally administered Fowler's solution will have a lower peak plasma

concentration with less cardiotoxicity in the form of cardiac arrhythmias than the same amount of arsenic trioxide administered intravenously.

When the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated. *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978) (Claims 1 and 6, directed to a method of effecting nonaddictive analgesia (pain reduction) in animals, were found to be anticipated by the applied prior art which disclosed the same compounds for effecting analgesia but which was silent as to addiction. The court upheld the rejection and stated that the applicants had merely found a new property of the compound and such a discovery did not constitute a new use. The court went on to reverse the rejection of claims 2-5 and 7-10 which recited a process of using a new compound. The court relied on evidence showing that the nonaddictive property of the new compound was unexpected.). See also *In re Tomlinson*, 363 F.2d 928, 150 USPQ 623 (CCPA 1966) (The claim was directed to a process of inhibiting light degradation of polypropylene by mixing it with one of a genus of compounds, including nickel dithiocarbamate. A reference taught mixing polypropylene with nickel dithiocarbamate to lower heat degradation. The court held that the claims read on the obvious process of mixing polypropylene with the nickel dithiocarbamate and that the preamble of the claim was merely directed to the result of mixing the two materials. "While the references do not show a specific recognition of that result, its discovery by appellants is tantamount only to finding a property in the old composition." 363 F.2d at 934, 150 USPQ at 628).

Claims 1-3, 5,6,9, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellison et al. (US 6,875,451) in view of Warrell, Jr. et al. (US Pat. 6,723,351).

Ellison et al. disclose oral administration and administration as a pill or tablet of arsenic trioxide (Claims 6, 10, 11). An embodiment is disclosed in which arsenic trioxide is dissolved in an aqueous solution of sodium hydroxide, with the pH adjusted to about 6-8 (Column 9, lines 33-36). A product of arsenic trioxide manufactured by Taylor Pharmaceuticals, Decatur, Ill. having a concentration of 1 mg/ml is disclosed (Column 16, lines 15-17). It is disclosed that the arsenic trioxide can be administered in combination with a therapeutically effective amount of at least one other therapeutic agent, such as a chemotherapeutic agent (Claims 3,5). It is disclosed that arsenic trioxide is effective in inhibiting the growth of leukemia cells in vitro and that arsenic trioxide can be used in human subject to treat a broad range of leukemia, including, acute lympocytic leukemia (myeloblastic, promyelocytic, myelomonocytic monocytic and erythroleukemia) and that for oral administration the pharmaceutical preparation can be in the form of solutions, suspensions, tablets and capsules (Column 12, lines 24-26, 47-66). It is disclosed that the magnitude of a therapeutic dose of an arsenic compound will vary with the severity of the condition treated and route of administration, age, body weight, condition and response of the individual patient and in general total daily dosage ranges are generally from about 10 micrograms to about 200 mg, preferable 0.5 to about 70 mg of the active ingredient (Column 14, lines 4-14).

Warrell, Jr. et al. disclose treatment of leukemia, including acute myeloblastic leukemia and acute promyelocystic leukemia with oral administration of arsenic trioxide, including in the form of solutions, suspensions, capsules and tablets, and in combination with chemotherapeutic agents (column 4, lines 40-68, Columns 5, 6, Column 9, lines 23-44). It is disclosed that arsenic trioxide is a solid inorganic compound that is commercially available in a very pure form (Column 8, lines 20-22). It is disclosed that the daily dose ranges from about 0.05 to about 5

mg/kg body weight administered and that the preferred total daily dose is from 2.5 to about 40 mg of arsenic trioxide (Column 10, lines 26-41). It is disclosed that the magnitude of therapeutic dose of arsenic compound in the acute or chronic management of leukemia will vary with the severity of the condition, route of administration, age, body weight, condition and response of individual patient Column 10, lines 20-26). It is disclosed that the arsenic compound can be as an active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques to prepare oral liquid preparations such as suspensions and solutions and oral solid preparations such as powders, capsules and tablets (Column 11, lines 36-52).

The prior art discloses arsenic trioxide in the form of solutions of having a concentration of arsenic trioxide of 1 mg/ml, pills and tablets. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose a tablet, capsule, dispersion or suspension where the arsenic trioxide is a powder, where the arsenic trioxide is a powder having a purity of at least 90%, 95%, 96%, 97%, 98%, 99% or where the arsenic trioxide tablet, capsule, dispersion or suspension which also contains or is combined with at least one other therapeutic agent, for example, a chemotherapeutic agent. However, the prior art amply suggests the same as the prior art discloses arsenic trioxide compositions in the form of powders, tablets, pills, capsules, solutions and suspensions, that arsenic trioxide is available in highly pure form and that oral arsenic trioxide can be used to treat leukemias, such as acute myeloid leukemia and acute promeylocytic leukemia. As such, one of ordinary skill in the art would have been motivated to modify and/or combine the prior art with the expectation that combination with other chemotherapeutic agents would enhance the effectiveness of the formulation against the leukemia condition treated and using an arsenic trioxide powder of very high purity avoid the

presence of undesired contaminates in the formulation and the use of a powder would facilitate the mixing of arsenic trioxide, where an intimate admixture is desired, with other ingredients, i.e. carriers or other active ingredients in liquid or powder form and that the oral arsenic trioxide would be effective in treating leukemias, such as acute myeloid leukemia and acute promeylocytic leukemia.

The Examiner has duly considered the Applicant's arguments but deems them moot in light of the new grounds of rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been taught by the teachings of the cited reference.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
March 21, 2008

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616